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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte TODD MANEGOLD and RICHARD G. ZIELINSKI

Appeal 2009-013003
Application 10/783,080
Technology Center 1600

Decided: July 1, 2010

Before CAROL A. SPIEGEL, TONI R. SCHEINER, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

SCHEINER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final rejection of claims 1-20, directed to an active-containing dissolvable film and a method of making it. The claims have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

STATEMENT OF THE CASE

Claims 1, 12 and 14 are representative of the claimed subject matter:

1. An active-containing dissolvable film prepared by solubilizing or dispersing an active ingredient in an aqueous environment, forming a mixture comprising the active ingredient and film-forming ingredients, coating the mixture onto a substrate material to form a film, and then drying the film to a moisture content of less than about 15 weight % moisture, said active ingredient having a water solubility of less than about 1 g/4mL at room temperature and being present in the film in amounts sufficient to impart a desired action upon administration of a single dosage form of the active-containing dissolvable film.

12. A method of making an active-containing dissolvable film comprising an active ingredient, the method comprising solubilizing or dispersing an active ingredient in an aqueous environment, forming a mixture of the dispersed or solubilized active ingredient and film-forming ingredients, coating the mixture onto a substrate material to form a film, and then drying the film to a moisture content of less than about 15 weight % moisture, said active ingredient having a water solubility of less than about 1 g/4mL at room temperature and used in amounts sufficient to impart a desired action upon administration of a single dosage form of the active-containing dissolvable film.

14. A dissolvable caffeine-containing film comprising at least about 18% by dry weight of caffeine based on the weight of said film.

The Examiner rejected the claims as follows:

- Claims 1-9 and 14-20 under 35 U.S.C. § 103(a) as unpatentable over Majeti[1] and Kulkarni.[2]

- Claims 1-20 under 35 U.S.C. § 103(a) as unpatentable over Ballard[3] and Kulkarni.

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[1] U.S. Patent 5,599,554, Majeti, issued February 4, 1997.
[2] WO 2004/096174 A1, Kulkarni et al., published November 11, 2004.

OBVIOUSNESS: Majeti and Kulkarni

Issue

Claim 1 is directed to a dissolvable film prepared by solubilizing or dispersing an active ingredient in an aqueous environment, mixing the solution or dispersion with film-forming ingredients, coating the mixture onto a substrate to form a film, and then drying the film to a moisture content of less than about 15%, wherein the active ingredient has a solubility of less than about 1 g/4mL at room temperature.

Independent claim 14 is directed to a dissolvable film comprising at least about 18% by dry weight of caffeine based in the weight of the film.

The issues raised by this rejection are whether the evidence of record supports the Examiner's conclusion that the prior art teaches or suggests:

a dissolvable film with a moisture content of less than about 15 weight % moisture, containing an active ingredient having a water solubility of less than about 1 g/4 mL at room temperature, present in the film in an amount sufficient to impart a desired action upon administration of a single dosage form of the dissolvable film as required by claim 1; and

a dissolvable film comprising at least about 18% by dry weight of caffeine based on the weight of the film, as required by claim 14.

Findings of Fact

FF1 According to the Specification, "[t]he active ingredient to be used in the practice of the invention is one having a water solubility of less than about 1g/4mL at room temperature" (Spec. 2). "Preferred are actives that are water soluble at some level, and includes actives that can only be

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[3] U.S. 2005/0013847 A1, Ballard et al., published January 20, 2005.

solubilized within a[n] aqueous environment upon agitation, upon the application of heat, upon a change in pH, or upon application of heat and/or agitation and/or pH change" (*id.* at 6).

FF2 The Specification teaches that "[s]pecific examples of active agents include . . . benzocaine, caffeine, dextromethorphan hydrobromide, guaifenesin, loratidine, L-theanine, ompremazole, pseudoephedrine hydrochloride, and vitamins like niacin or retinol" (*id.* at 9).

FF3 In addition, the Specification teaches that

> Water soluble solid film-forming agents conventionally used in the dissolvable film-forming art can be used in the current invention. Such water soluble polymers include . . . pullulan, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, polyvinyl pyrrolidone, carboxymethyl cellulose, polyvinyl alcohol, sodium alginate, polyethylene glycol, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymer, carboxyvinyl polymer, amylose, high amylose starch, hydroxypropylated high amylose starch, dextrin, pectin, chitin, chitosan, levan, elsinan, collagen, gelatin, zein, gluten, soy protein isolate, whey protein isolate, casein and various mixtures thereof.

(*Id.* at 10.)

FF4 Kulkarni discloses "a consumable film adapted to adhere to and dissolve in the mouth of a consumer including at least one water soluble polymer, at least one antitussive agent and a mucosa-coating effective amount of a mucosa-coating agent" (Kulkarni 3: 15-18).

FF5 Kulkarni's antitussive agent "is employed in an effective amount" (Kulkarni 6: 18-19), "adjusted to deliver a predetermined dose of the antitussive agent over a predetermined period of time, which may typically vary from 4 to 24 hours" (*id.* at 7: 6-8).

> Except as otherwise noted, the amount of [the] antitussive agent in the consumable film . . . is designated as % by weight after the "wet" film formulation has been dried and formed into the consumable film. Generally, the amount of the antitussive agent used in the consumable film is from about 0.01% to about 80% by weight based on the total weight of the consumable film, preferably from about 2.5% to about 40% by weight, and more preferably from about 5% to about 30% by weight.

(*Id.* at 7: 16-22.)

FF6 The antitussive agent in all of Kulkarni's working examples is dextromethorphan hydrobromide, and its weight percentage in the "[a]ctual batch[es]" ranges from 5.5038 to 10.6759, and from 18.3460 to 27.3219 in the dry film, "[a]ssuming that all water is evaporated" (*id.* at Examples 1-15).

FF7 Kulkarni teaches that

> Useful water soluble polymers that exhibit film forming properties include pullulan, hydroxypropylmethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, polyvinyl pyrrolidone, carboxymethyl cellulose, polyvinyl alcohol, sodium alginate, polyethylene glycol, tragacanth gum, guar gum, acacia gum, arabic gum, polyacrylic acid, methylmethacrylate copolymers, carboxyvinyl polymers, amylose, high amylose starch, hydroxypropylated high amylose starch, dextrin, chitin, chitosan, levan, elsinan, collagen, zein, gluten, soy protein isolate, whey protein isolate, casein and combinations thereof.

(*Id.* at 10: 12-19). In addition, "[s]uitable mucosa-coating agents include pectin, gelatin, and the like, and combinations thereof" (*id.* at 5: 19-20).

FF8 Kulkarni teaches that "[a]dditional therapeutic agents that are effective for treating conditions other than coughing may be added . . . such

as an antihistamine" (Kulkarni 8: 4-6), and "[u]seful antihistamines include . . . loratadine" (*id.* at 8: 13). In addition, "[t]he film compositions . . . may also be used to supply nutritionally acceptable components such as vitamins" (*id.* at 9: 3-4), including niacin (*id.* at 9: 9).

FF9 Kulkarni's dissolvable films are made by

> preparing an aqueous phase comprising a mucosa-coating effective amount of a mucosa-coating agent; preparing a film-forming mixture including at least one water soluble polymer; combining the aqueous phase and the film forming mixture to form a hydrated polymer gel; casting the hydrated polymer gel on a substrate to form a cast gel; and drying the cast gel to form the consumable film, wherein the at least one antitussive agent is added to the aqueous phase, the hydrated polymer gel or both.

(*Id.* at 2: 21 to 3: 5.)

FF10 Kulkarni teaches that "[t]he consumable film is preferably air-dried and dried under warm air and cut to a desired dimension, packaged and stored. The packaged film may contain moisture in amounts of from about 0.1% to about 10% by weight, and more preferably from about 4% to about 7% by weight" (*id.* at 14: 21 to 15: 2).

FF11 Majeti discloses nicotine- and caffeine-containing "transdermal and buccal patches, bioadhesive and mucoadhesive films . . . suitable [for] administering the . . . compositions transdermally and/or transmucosally" (Majeti, col. 3, ll. 4, 17, and 40-43).

FF12 Majeti teaches that caffeine is "slightly soluble in water and alcohol" (*id.* at col. 3, l. 20).

FF13 Majeti teaches that the compositions are "prepared in dosage unit form to contain safe and effective amounts of the nicotine and caffeine

. . . to achieve the desired blood levels" (*id.* at col. 4, ll. 3-6), and the amount and "may vary depending on the carrier chosen and the personal needs of the user" (*id.* at col. 4, ll. 25-26).

Principles of Law

"The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007).

Analysis

Claims 1-9 and 16-20

Appellants do not argue claims 1-9 and 16-20 separately. We select claim 1 as representative, and claims 2-9 and 16-20 will stand or fall with claim 1. 37 C.F.R. § 41.37(c)(1)(vii).

Claim 1 is directed to a dissolvable film with "a moisture content of less than about 15 weight % moisture" and containing an "active ingredient having a water solubility of less than about 1 g/4 mL at room temperature . . . present in the film in amounts sufficient to impart a desired action upon administration of a single dosage form of the active-containing dissolvable film."

The Examiner finds that Majeti discloses "transdermally or transmucosally administrable composition[s] in the form of mucoadhesive or bioadhesive films . . . compris[ing] caffeine, which is slightly soluble in water and alcohol" (Ans. 4), but doesn't disclose "the claimed percentage or amount of caffeine" in the compositions (*id.*). However, the Examiner finds that Kulkarni discloses "fast dissolving orally consumable films containing pharmaceutically active agents" (*id.* at 5), and particularly discloses films containing dextromethorphan hydrobromide (*id.*). The Examiner concludes

that it would have been obvious "to prepare an active containing dissolvable film based on the teachings and guidance provided by Kulkarni and Majeti" (*id.*), "in order to achieve the claimed orally dissolvable film" (*id.*).

Appellants contend that "[t]here is no disclosure of a dissolvable film in Majeti, or that any active, let alone actives that are not very soluble like caffeine, may be administered using a dissolvable film" (App. Br. 5). Appellants acknowledge that "Kulkarni discloses dissolvable films," but contend the reference "is silent as to whether actives having low levels of solubility can be incorporated into a dissolvable film at levels where they exert a desired effect when administered" (*id.*).

Appellants' arguments are not persuasive. As noted by the Examiner, Kulkarni discloses dissolvable, orally consumable films containing various active agents (Ans. 5). While Kulkarni doesn't discuss the water solubility of its active agents per se, its working examples contain dextromethorphan hydrobromide in various concentrations (FF6). The present Specification states that "[t]he active ingredient to be used in the practice of the invention is one having a water solubility of less than about 1g/4mL at room temperature" (Spec. 2; FF1), and explicitly discloses dextromethorphan hydrobromide as a suitable active agent (Spec. 9; FF2). Moreover, Kulkarni teaches that its active agents are included in the dissolvable films in effective amounts (FF5).

Given these facts, we agree with the Examiner that the prior art teaches or suggests a dissolvable film with a moisture content of less than about 15 weight % moisture, containing an active ingredient having a water solubility of less than about 1 g/4 mL at room temperature, present in the film in an effective amount, as required by claim 1.

Claims 14 and 15

Independent claim 14 is directed to a dissolvable caffeine-containing film comprising at least about 18% by dry weight of caffeine based on the weight of the film.

Appellants contend that "there is nothing in the combined disclosures of Majeti and Kulkarni to suggest that caffeine, in the amounts required in claims 14 and 15, could be administered using a dissolvable film" (App. Br. 6).

Nevertheless, we agree with the Examiner that it would have been obvious for one skilled in the art to include caffeine in Kulkarni's dissolvable film, given the fact that Kulkarni discloses dissolvable, mucoadhesive films suitable for transmucosal delivery of various effective amounts of active agents (including dextromethorphan hydrobromide, one of Appellants' slightly soluble actives) (FF1, 2, 6), and the fact that that Majeti teaches that mucoadhesive films are appropriate vehicles for transmucosal delivery of caffeine (FF11), a slightly water soluble compound (FF12). "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR*, 550 U.S. at 416. That is the case here.

With respect to the concentration of caffeine in the dissolvable film, Majeti teaches that the amount of caffeine included in the transmucosal or transdermal delivery vehicle varies depending on the carrier and the needs of the user (FF13). Similarly, Kulkarni demonstrates that dextromethorphan hydrobromide can be incorporated into consumable, dissolvable films in various effective amounts, and that the final percentage can vary over a wide range depending on the desired dosage and the amount of water remaining in

the film after drying. It is well settled that "'it is not inventive to discover the optimum or workable ranges by routine experimentation.' Only if the 'results of optimizing a variable' are 'unexpectedly good' can a patent be obtained for the claimed critical range." *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997) (citations omitted). Appellants have not established that including the required percentage weight of caffeine in a dissolvable film would have required anything more than routine, empirical experimentation, or that films containing the required amount have any unexpected properties.

Conclusions of Law

The evidence of record supports the Examiner's conclusion that the prior art teaches or suggests:

a dissolvable film with a moisture content of less than about 15 weight % moisture, containing an active ingredient having a water solubility of less than about 1 g/4 mL at room temperature, present in the film in an amount sufficient to impart a desired action upon administration of a single dosage form of the dissolvable film as required by claim 1; and

a dissolvable film comprising at least about 18% by dry weight of caffeine based on the weight of the film as required by claim 14.

OBVIOUSNESS: Ballard and Kulkarni

Issue

The issue raised by this rejection is whether the evidence of record supports the Examiner's conclusion that the prior art teaches or suggests:

a dissolvable film with a moisture content of less than about 15 weight % moisture, containing an active ingredient having a water solubility of less than about 1 g/4 mL at room temperature, present in the film in an amount

sufficient to impart a desired action upon administration of a single dosage form of the dissolvable film as required by claim 1;

a dissolvable film wherein the film-forming ingredients comprise a modified starch, as required by claim 10;

a dissolvable film comprising at least about 18% by dry weight of caffeine based on the weight of the film, as required by claim 14; and

applying the dissolvable film of claim 1 to traumatized tissue, as required by claim 18.

Findings of Fact

FF14 Ballard discloses

> [A] delivery system comprising a homogenous, thermoreversible gel film, wherein said gel film comprises: (i) a film forming amount of a water soluble thermoreversible alginate and optionally at least one of a plasticizer, a second film former, a bulking agent, and a pH controlling agent; an (ii) an active substance.

(Ballard ¶ 6.)

FF15 Ballard's bulking agents include various starches, particularly modified starches (Ballard ¶ 24).

FF16 Examples of suitable active substances for Ballard's films include "an oral care agent, a breath freshening agent, a pharmaceutical agent, a nutraceutical agent, a salivary stimulant agent, a vitamin, a mineral, a coloring agent, cosmetic ingredient, agricultural active, a sweetener, a flavorant, a fragrance or a food" (Ballard ¶ 18). In addition, Ballard discloses thermoreversible gels containing caffeine (*id.* at ¶¶ 100, 102).

FF17 Ballard discloses that "[t]he gel films . . . have a solids content of at least 50%, at least 60%, at least 70%, at least 80% and at least 90% of

all components in the gel film" and "up to 15%, 10% or 5% water may remain strongly associated with the solids in the dry gel film" (Ballard ¶ 28).

Analysis

Claims 1-9, 12, 13, 16, 17, and 20

Appellants don't argue claims 1-9, 12, 13, 16, 17, and 20 separately; again, we select claim 1 as representative of this group of claims for purposes of deciding the issues raised by this rejection.

The Examiner finds that Ballard discloses "a delivery system comprising a homogenous, thermoreversible gel film comprising film formers, [and an] active substance" (Ans. 6), one of which is caffeine (*id.*), but doesn't disclose "the claimed percentage or amount of caffeine" in the compositions (*id.* at 7). Again, the Examiner finds that Kulkarni discloses "fast dissolving orally consumable films containing pharmaceutically active agents" (*id.* at 6), and discloses "preparing a supple, non-self adhering film especially suitable for oral delivery of active ingredient[s]" (*id.* at 7), particularly dextromethorphan hydrobromide (*id.*). The Examiner concludes that it would have been obvious "to prepare an active containing dissolvable film based on the teachings and guidance provided by Kulkarni and Ballard" (*id.*), "in order to achieve the claimed orally dissolvable film" (*id.*).

Appellants acknowledge that "Ballard and Kulkarni disclose[ ] films useful in administering actives," but contend "there is no disclos[ure] or suggestion that actives having low levels of solubility can be incorporated into a dissolvable film at levels where a desired effect is obtained following administration" (App. Br. 7).

Appellants' arguments are not persuasive. Again, as noted by the Examiner, Kulkarni discloses dissolvable, orally consumable films

containing various active agents (Ans. 5). While Kulkarni doesn't discuss the water solubility of its active agents per se, its working examples contain dextromethorphan hydrobromide in various concentrations (FF6). The present Specification states that "[t]he active ingredient to be used in the practice of the invention is one having a water solubility of less than about 1g/4mL at room temperature" (Spec. 2; FF1), and explicitly discloses dextromethorphan hydrobromide as an active agent (Spec. 9; FF2). Moreover, Kulkarni teaches that its active agents are included in the dissolvable films in effective amounts (FF5).

Given these facts, we agree with the Examiner that the prior art teaches or suggests a dissolvable film with a moisture content of less than about 15 weight % moisture, containing an active ingredient having a water solubility of less than about 1 g/4 mL at room temperature, present in the film in an effective amount, as required by claim 1.

Claims 10 and 11

Claim 10 depends from claim 1 and specifies that the "film-forming ingredients comprise a starch component comprising at least about 85% modified starch." Claim 11 limits the modified starch to a hydroxyalkylated starch or a succinated starch.

Appellants contend that "there is nothing in the combined disclosures of Ballard and Kulkarni to suggest that caffeine, which has a low solubility level, could be administered in amounts effective to impart a desired action using a dissolvable film that comprises starch" (App. Br. 7).

First, Kulkarni specifically teaches that starches, including hydroxypropylated high amylose starch, are appropriate film-forming agents for dissolvable films (FF7), and Ballard discloses starches as bulking agents

in gel films (FF15). Moreover, as discussed above, we agree with the Examiner that it would have been obvious for one skilled in the art to include caffeine in Kulkarni's dissolvable film, given the fact that Kulkarni discloses dissolvable, mucoadhesive films suitable for transmucosal delivery of various effective amounts of active agents (including dextromethorphan hydrobromide, one of Appellants' slightly soluble actives) (FF1, 2, 6), and the fact that that Ballard teaches that films are appropriate vehicles for oral delivery of caffeine (FF16), a slightly water soluble compound (FF12).

Claims 14 and 15

Independent claim 14 is directed to a dissolvable caffeine-containing film comprising at least about 18% by dry weight of caffeine based on the weight of the film.

Appellants contend that "there is nothing in the combined disclosures of Ballard and Kulkarni to suggest that caffeine, in the amounts required in claims 14 and 15, could be administered using a dissolvable film" (App. Br. 8).

Again, we agree with the Examiner that it would have been obvious for one skilled in the art to include caffeine in Kulkarni's dissolvable film, given the fact that Kulkarni discloses dissolvable, mucoadhesive films suitable for transmucosal delivery of various effective amounts of active agents (including dextromethorphan hydrobromide, one of Appellants' slightly soluble actives) (FF1, 2, 6), and the fact that that Ballard teaches that films are appropriate vehicles for oral delivery of caffeine (FF16), a slightly water soluble compound (FF12). Moreover, we agree with the Examiner that the required concentration of caffeine would have been obvious for the reasons discussed above.

Claims 18 and 19

Claim 18 is directed to a method of administering the dissolvable film of claim 1 by applying it to traumatized tissue; claim 19 depends from claim 18 and specifies that the traumatized tissue is skin.

Appellants contend that "[t]here is no disclosure of administering actives . . . by application of a film to traumatized tissue in either of Ballard or Kulkarni" (App. Br. 8), thus, "their combination also fails to suggest the claimed subject matter" (*id.* at 8-9).

We agree with Appellants that the Examiner has not explained why Ballard's disclosure of films for oral delivery of actives, and Kulkarni's disclosure of films for transmucosal delivery of actives would have suggested applying the films to traumatized tissue.

Conclusions of Law

The evidence of record supports the Examiner's conclusion that the prior art teaches or suggests:

a dissolvable film with a moisture content of less than about 15 weight % moisture, containing an active ingredient having a water solubility of less than about 1 g/4 mL at room temperature, present in the film in an amount sufficient to impart a desired action upon administration of a single dosage form of the dissolvable film as required by claim 1;

a dissolvable film wherein the film-forming ingredients comprise a modified starch, as required by claim 10; and

a dissolvable film comprising at least about 18% by dry weight of caffeine based on the weight of the film, as required by claim 14.

However, the Examiner has not established that the teachings of Ballard and Kulkarni teach or suggest applying the dissolvable film of claim 1 to traumatized tissue, as required by claim 18.

SUMMARY

- The rejection of claims 1-9 and 14-20 under 35 U.S.C. § 103(a) as unpatentable over Majeti and Kulkarni is affirmed.
- The rejection of claims 1-20 under 35 U.S.C. § 103(a) as unpatentable over Ballard and Kulkarni is affirmed with respect to claims 1-17 and 20, and reversed with respect to claims 18 and 19.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv)(2006).

AFFIRMED

alw

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